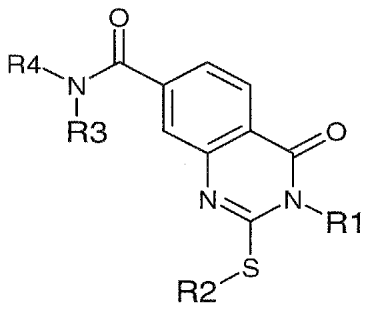
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable diluent or carrier and an active ingredient of the general formula I:



wherein:

R_1 is optionally substituted hydrocarbyl or heterocyclyl;

R_2 is selected from the group consisting of H, $(C_1$-$C_{12})$alkyl, $(C_6$-$C_{14})$aryl-CH_2-, heteroaryl-CH_2-, alkylcarbonyl-CH_2-, $(C_6$-$C_{14})$arylcarbonyl-CH_2- and heteroarylcarbonyl-CH_2-;

R_3 and R_4 each is selected from the group consisting of hydrogen, C_1-C_6 alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, and C_1-C_6 alkyl substituted by a group containing a basic nitrogen atom or by a 5-7 membered heterocyclic ring containing one or two heteroatoms, one of them being a basic nitrogen atom, or R_3 and

R_4 together with the nitrogen atom to which they are attached form a 5-7 membered saturated heterocyclic ring containing one or two basic nitrogen atoms, optionally substituted on the additional nitrogen atom;

and pharmaceutically acceptable salts thereof.

Claims 2-17 (Cancelled).

18. (Currently Amended) The pharmaceutical composition according to claim ~~1~~ 85, wherein the compound of formula I is selected from the group consisting of:

2-[[(4-chlorophenyl)methyl]thio]-3-(4-fluorophenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide [Compound No. 1];

2-[[(4-methylphenyl)methyl]thio]-3-(4-fluorophenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide [Compound No. 2];

2-[[(3-fluorophenyl)methyl]thio]-3-(4-fluorophenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide [Compound No. 3];

~~2-[(2-oxo-2-phenylethyl)thio]-3-(4-fluorophenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide [Compound No. 5];~~ and

2-[[2-[[(3-chlorophenyl)methyl]thio]-3-pentyl-3,4-dihydro-4-oxo-N-(4-methylpiperazinyl)-7-quinazolinecarboxamide [Compound No. 4].

19. (Currently Amended) The pharmaceutical composition according to claim ~~1~~ 85 wherein the compound of formula I is 2-[[(6-nitro-4H-1,3-benzodioxin-8-yl)methyl]thio]-3-(2-propenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide (Compound No. 2010).

20. (Currently Amended) The pharmaceutical composition according to claim ~~1~~ 85 wherein the compound of formula I is 2-[[(5-acetyl-2-methoxyphenyl)methyl)thio]-3-(phenylmethyl)-3,4-dihydro-4-oxo-N-[3-(1H-imidazol-1-yl)propyl]-7-quinazolinecarboxamide (Compound No. 2011).

21. (Currently Amended) The pharmaceutical composition according to claim ~~1~~ 85, wherein the compound of formula I is 2-[[(5-acetyl-2-methoxyphenyl)methyl]thio]-3-(phenylmethyl)-3,4-dihydro-4-oxo-N-(1-ethyl-piperidin-4-yl)-7-quinazoline-carboxamide (Compound No. 2012).

22. (Currently Amended) The pharmaceutical composition according claim ~~1~~ 85, for the treatment or prevention of inflammatory or autoimmune diseases, disorders

or conditions related to cell adhesion or cell migration mediated by heparan sulfate glycosaminoglycans (HS-GAGs).

Claims 23-28 (Cancelled).

29. (Currently Amended) The pharmaceutical composition according to claim ~~1~~ 85, for modulating the anticoagulant activity of glycosaminoglycans.

30. (Original) The pharmaceutical composition according to claim 29, wherein the glycosaminoglycan is heparin.

31. (Currently Amended) The pharmaceutical composition according to claim ~~1~~ 85, capable of inhibiting the interaction of glycosaminoglycans with selectins.

32. (Currently Amended) The pharmaceutical composition according to claim ~~1~~ 85, capable of inhibiting neutrophil infiltration in vivo.

Claims 33-42 (Cancelled).

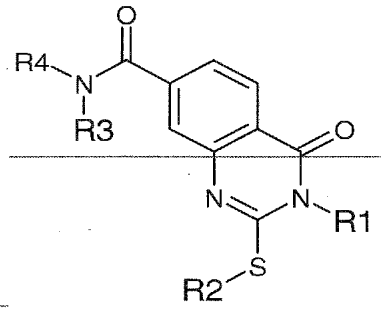
43. (Original) The compound 2-[[(6-nitro-4H-1,3-benzodioxin-8-yl)methyl]thio]-3-(2-propenyl)-3,4-dihydro-4-

oxo-N-[3-(4-morpholinyl)propyl]-7-quinazoline carboxamide (Compound No. 2010).

44. (Original) The compound 2-[[(5-acetyl-2-methoxyphenyl) methyl)thio]-3-(phenyl-methyl)-3,4-dihydro-4-oxo-N-[3-(1H-imidazol-1-yl)propyl]-7-quinazoline-carboxamide (Compound No. 2011).

45. (Original) The compound 2-[[(5-acetyl-2-methoxyphenyl) methyl]thio]-3-(phenyl-methyl)-3,4-dihydro-4-oxo-N-(1-ethyl-piperidin-4-yl)-7-quinazolinecarboxamide (Compound No. 2012).

46. (Currently Amended) A method for the treatment or prevention of diseases, disorders or conditions related to cell adhesion or cell migration mediated by heparan sulfate glycosaminoglycans, comprising the step of administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a compound of the general formula I in claim 85.



wherein:

R_1 is optionally substituted hydrocarbyl or heterocyclyl;

R_2 is selected from the group consisting of H, (C_1-C_{12})alkyl, (C_6-C_{14})aryl-CH_2-, heteroaryl-CH_2-, alkylcarbonyl-CH_2-, (C_6-C_{14})arylcarbonyl-CH_2-, and heteroarylcarbonyl-CH_2-;

R_3 and R_4 each is selected from the group consisting of hydrogen, C_1-C_6 alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, and C_1-C_6 alkyl substituted by a group containing a basic nitrogen atom or by a 5-7 membered heterocyclic ring containing one or two heteroatoms, one of them being a basic nitrogen atom, or R_3 and R_4 together with the nitrogen atom to which they are attached form a 5-7 membered saturated heterocyclic ring containing one or two basic nitrogen atoms, optionally substituted on the additional nitrogen atom;

and pharmaceutically acceptable salts thereof.

Claims 47-62 (Cancelled).

63. (Currently Amended) The method according to claim 46, wherein the compound of formula I is selected from the group consisting of:

2-[[(4-chlorophenyl)methyl]thio]-3-(4-fluorophenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide [Compound No. 1];

2-[[(4-methylphenyl)methyl]thio]-3-(4-fluorophenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide [Compound No. 2];

2-[[(3-fluorophenyl)methyl]thio]-3-(4-fluorophenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide [Compound No. 3];

~~2-[(2-oxo-2-phenylethyl)thio]-3-(4-fluorophenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide [Compound No. 5]; and~~

2-[[2-[[(3-chlorophenyl)methyl]thio]-3-pentyl-3,4-dihydro-4-oxo-N-(4-methylpiperazinyl)-7-quinazolinecarboxamide [Compound No. 4].

64. (Original) The method according to claim 46, wherein the compound of formula I is 2-[[(6-nitro-4H-1,3-benzodioxin-8-yl)methyl]thio]-3-(2-propenyl)-3,4-dihydro-4-oxo-N-[3-(4-morpholinyl)propyl]-7-quinazolinecarboxamide (Compound No. 2010).

65. (Original) The method according to claim 46, wherein the compound of formula I is 2-[[(5-acetyl-2-methoxyphenyl)methyl)thio]-3-(phenylmethyl)-3,4-dihydro-4-oxo-N-[3-(1H-imidazol-1-yl)propyl]-7-quinazolinecarboxamide (Compound No. 2011).

66. (Original) The method according to claim 46, wherein the compound of formula I is 2-[[(5-acetyl-2-methoxyphenyl)methyl]thio]-3-(phenylmethyl)-3,4-dihydro-4-oxo-N-(1-ethyl-piperidin-4-yl)-7-quinazoline-carboxamide (Compound No. 2012).

Claims 67-72 (Cancelled).

73. (Original) A method for modulating the anticoagulant activity of glycosaminoglycans which comprises administering to a subject in need a therapeutically effective amount of a compound of the general formula I in claim 46.

74. (Original) The method according to claim 73, wherein the glycosaminoglycan is heparin.

75. (Currently Amended) The pharmaceutical composition according to claim ~~1~~ 85, wherein

R_1 is a hydrocarbyl selected from the group consisting of C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkenyl, C_6-C_{14} aryl, (C_1-C_6)alkyl(C_6-C_{14})aryl, and (C_6-C_{14})aryl(C_1-C_{12})alkyl, or such a hydrocarbyl substituted by at least one radical selected from the group consisting of C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_7-C_{12} aralkyl, C_6-C_{10} aryl, C_7-C_{12} alkaryl, hydroxy, C_1-C_{10} alkoxy, C_6-C_{10} aryloxy, C_1-C_{10} alkylthio, C_6-C_{10} arylthio, C_6-C_{10} arylamino, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkenyl, amino, C_1-C_{10} alkylamino, di(C_1-C_{10})-alkylamino, C_2-C_{12} alkoxyalkyl, C_2-C_{12} alkylthioalkyl, C_1-C_{10} alkylsulfinyl, C_1-C_{10} alkylsulfonyl, C_6-C_{10} arylsulfonyl, hydroxy(C_1-C_{10})alkyl, (C_6-C_{10})aryloxy(C_1-C_{10})alkyl, (C_1-C_{10})alkoxycarbonyl, (C_6-C_{10})aryloxycarbonyl, C_2-C_{11} alkanoyl, (C_7-C_{11})aroyl, fluoro(C_1-C_{10})alkyl, oxo, nitro, nitro(C_1-C_{10})alkyl, cyano, cyano(C_1-C_{10})alkyl, aminocarbonyl, (C_1-C_{10})alkylaminocarbonyl, di(C_1-C_{10})-alkylaminocarbonyl, aminocarbonyl(C_1-C_{10})alkyl, aminocarbonyl(C_6-C_{10})aryl, aminosulfonyl, (C_1-C_{10})alkylaminosulfonyl, di(C_1-C_{10})-alkylaminosulfonyl, amidino, carboxy, sulfo, heterocyclyl, and -$(CH_2)_m$-Z-(C_1-C_{10} alkyl), where m is 1 to 8 and Z is oxygen or sulfur; or R_1 is a heterocyclyl radical derived from a mono- or poly-cyclic ring containing one to three heteroatoms selected from the group consisting of N, O and S;

R_2 is selected from the group consisting of (C_6-C_{14})aryl-CH_2-, (C_6-C_{14})arylcarbonyl-CH_2-, heteroaryl-CH_2- and heteroarylcarbonyl-CH_2-, wherein said aryl or heteroaryl is unsubstituted or substituted by at least one radical selected from the group consisting of C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_7-C_{12} aralkyl, C_6-C_{10} aryl, C_7-C_{12} alkaryl, hydroxy, C_1-C_{10} alkoxy, C_6-C_{10} aryloxy, C_1-C_{10} alkylthio, C_6-C_{10} arylthio, C_6-C_{10} arylamino, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkenyl, amino, C_1-C_{10} alkylamino, di(C_1-C_{10})-alkylamino, C_2-C_{12} alkoxyalkyl, C_2-C_{12} alkylthioalkyl, C_1-C_{10} alkylsulfinyl, C_1-C_{10} alkylsulfonyl, C_6-C_{10} arylsulfonyl, hydroxy(C_1-C_{10})alkyl, (C_6-C_{10})aryloxy(C_1-C_{10})alkyl, (C_1-C_{10})alkoxycarbonyl, (C_6-C_{10})aryloxycarbonyl, C_2-C_{11} alkanoyl, (C_7-C_{11})aroyl, fluoro(C_1-C_{10})alkyl, oxo, nitro, nitro(C_1-C_{10})alkyl, cyano, cyano(C_1-C_{10})alkyl, aminocarbonyl, (C_1-C_{10})alkylaminocarbonyl, di(C_1-C_{10})-alkylaminocarbonyl, aminocarbonyl(C_1-C_{10})alkyl, aminocarbonyl(C_6-C_{10})aryl, aminosulfonyl, (C_1-C_{10})alkylaminosulfonyl, di(C_1-C_{10})-alkylaminosulfonyl, amidino, carboxy, sulfo, heterocyclyl, and -$(CH_2)_m$-Z-(C_1-C_{10} alkyl), where m is 1 to 8 and Z is oxygen or sulfur; and wherein said heteroaryl is selected from the group consisting of pyrrolyl, furyl, thienyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl thiazolyl, isothiazolyl, pyridyl, 1,3-benzodioxanyl, pyrazinyl, pyrimidinyl, 1,3,4-triazinyl, 1,2,3-triazinyl, 1,3,5-triazinyl, thiazinyl, quinolinyl,

isoquinolinyl, benzofuryl, isobenzofuryl, indolyl, imidazo[1,2-a]pyridyl, pyrido[1,2-a]pyrimidinyl, benzimidazolyl, benzthiazolyl, and benzoxazolyl;

R_3 is hydrogen; and

R_4 is selected from the groups consisting of:

(i) (C_1-C_6)alkoxy(C_1-C_6)alkyl;

(ii) (C_1-C_6)alkyl substituted by a group selected from the group consisting of an amino group $-NR_5R_6$, an ammonium group $-N^+(R_5R_6R_7)$, a hydrazine group $-NR_5-NR_6R_7$, a hydrazonium group $-NR_5-N^+(R_6R_7R_8)$, an ammoniumoxy group $-O-N^+(R_5R_6)$, an imine group $-C=NR_5R_6$, an iminium group $-C=N^+(R_5R_6R_7)$, a guanidine group $-NR_5-C(=NH)-NR_6R_7$, and a guanidinium group $-NR_5-C(=NH)-N^+(R_6R_7R_8)$, wherein each of R_5, R_6, R_7 and R_8 is H, or optionally substituted C_1-C_{10} alkyl or C_6-C_{10} aryl, but excluding a tertiary amino group $-NR_5R_6$, wherein R_5 and R_6 are C_1-C_6 alkyl; and

(iii) (C_1-C_6)alkyl substituted by a 5-7 membered heterocyclic ring selected from the group consisting of pyrrolidine, pyrroline, pyrrol, imidazolidine, imidazoline, imidazole, ~~piperidine~~, dihydropyridine, tetrahydropyridine, pyridine, 1,2-pyrazine, tetrahydropyrimidine, dihydropyrimidine, pyrimidine, 1,4-pyrazine, 1,4-tetrahydropyrazine, 1,4-dihydropyrazine, piperazine, diazepine, oxazolidine, oxazoline, oxazole, morpholino, 1,4-dihydrooxazine, 1,4-oxazine. thiazolidine, thiazoline,

thiaazole, thiomorpholino, 1,4-dihydrothiazine, and 1,4-thiazine; or

R_3 and R_4 together with the nitrogen atom to which they are attached form a 5-7 membered saturated heterocyclic ring containing one or two basic nitrogen atoms selected from the group consisting of pyrrolidine, imidazolidine, piperidine, piperazine, and piperazine substituted at the additional nitrogen atom by C_1-C_6 alkyl or by C_1-C_6 alkyl substituted by halo, hydroxy, C_1-C_6 alkoxy or C_6-C_{10} aryl, or C_2-C_7 alkoxycarbonyl.

76. (Currently Amended) The pharmaceutical composition according to claim 75, wherein R_1 is selected from the group consisting of pentyl, allyl, phenyl, 4-fluorophenyl, benzyl, 2-furylmethyl and (tetrahydro-2-furyl)methyl;
R_2 is selected from the group consisting of phenyl-CH_2-, 4-methylphenyl-CH_2-, 3-fluorophenyl-CH_2-, 4-fluorophenyl-CH_2-, 3-chlorophenyl-CH_2-, 4-chlorophenyl-CH_2-, phenylcarbonyl-CH_2-, 4-fluoro-phenylcarbonyl-CH_2-, 4-chloro-phenylcarbonyl-CH_2-, 4-pyridyl-CH_2- and 4-oxo-4H-pyrido[1,2-a]pyrimidin-yl-CH_2-;

R_3 is hydrogen; and

R_4 is selected from the group consisting of 2-methoxyethyl, 3-(4-morpholinyl)propyl and ~~3-(1-piperidinyl)propyl~~; or

R_3 and R_4 together with the nitrogen atom to which they are attached form 4-methylpiperazinyl or 1- piperazinyl-4-carboxylic acid ethyl ester.

77. (Previously Presented) The pharmaceutical composition according to claim 22, wherein said inflammatory or autoimmune disease, disorder or condition is selected from the group consisting of sepsis, wound associated sepsis, post-septic shock, ischemic leukocyte-mediated tissue damage (ischemia-reperfusion injury) such as myocardial ischemia, platelate-mediated pathologies such as atherosclerosis and clotting, cardiomyopathic disease, stroke, restenosis, infectious meningitis, encephalitis, allergic conjunctivitis, organ/tissue transplant rejection (such as skin, kidney, heart, lung, liver, bone marrow, cornea, pancreas, small bowel, autologous bone marrow transplantation), "graft versus host" disease (GVHD), lupus, frost-bite injury or shock, acute leukocyte-mediated lung injury (such as adult respiratory distress syndrome), asthma, allergic rhinitis, acute pancreatitis, traumatic shock, traumatic brain injury, acute and chronic inflammation such as atopic dermatitis, psoriasis, contact dermal hypersensitivity and inflammatory bowel disease such as Crohn's disease and ulcerative colitis, rheumatoid arthritis, retinitis; multiple sclerosis; amyloid disorders

such as Alzheimer's disease and type II diabetes; angiogenesis pathologies selected from the group consisting of tumor angiogenesis, ophthalmologic disorders such as neovascular glaucoma, diabetic retinopathy, macular degeneration (particularly age-related macular degeneration) and uveitis, reperfusion of gastric ulcer, contraception and inducing abortion at early stages of pregnancy; viral disorders selected from the group consisting of hepatitis C, hepatitis B, influenza, rhinovirus infections, cytomegalovirus infections, AIDS and respiratory syncytial virus infections; bone degradation, osteoporosis, osteoarthritis, kidney disease including glomerulonephritis and nephritis; and bacterial infections.

78. (Previously Presented) The pharmaceutical composition according to claim 22, wherein said disease is cancer or tumor metastasis.

79. (Previously Presented) The pharmaceutical composition according to claim 31, wherein said selectin is L-selectin.

80. (Currently Amended) The method according to claim 46, wherein

R_1 a is hydrocarbyl selected from the group consisting of C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkenyl, C_6-C_{14} aryl, (C_1-C_6)alkyl(C_6-C_{14})aryl, and (C_6-C_{14}) aryl(C_1-C_{12})alkyl, or such a hydrocarbyl substituted by at least one radical selected from the group consisting of C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_7-C_{12} aralkyl, C_6-C_{10} aryl, C_7-C_{12} alkaryl, hydroxy, C_1-C_{10} alkoxy, C_6-C_{10} aryloxy, C_1-C_{10} alkylthio, C_6-C_{10} arylthio, C_6-C_{10} arylamino, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkenyl, amino, C_1-C_{10} alkylamino, di(C_1-C_{10})-alkylamino, C_2-C_{12} alkoxyalkyl, C_2-C_{12} alkylthioalkyl, C_1-C_{10} alkylsulfinyl, C_1-C_{10} alkylsulfonyl, C_6-C_{10} arylsulfonyl, hydroxy(C_1-C_{10})alkyl, (C_6-C_{10})aryloxy(C_1-C_{10})alkyl, (C_1-C_{10})alkoxycarbonyl, (C_6-C_{10})aryloxycarbonyl, C_2-C_{11} alkanoyl, (C_7-C_{11})aroyl, fluoro(C_1-C_{10})alkyl, oxo, nitro, nitro(C_1-C_{10})alkyl, cyano, cyano(C_1-C_{10})alkyl, aminocarbonyl, (C_1-C_{10})alkylaminocarbonyl, di(C_1-C_{10})-alkylaminocarbonyl, aminocarbonyl(C_1-C_{10})alkyl, aminocarbonyl(C_6-C_{10})aryl, aminosulfonyl, (C_1-C_{10})alkylaminosulfonyl, di(C_1-C_{10})-alkylaminosulfonyl, amidino, carboxy, sulfo, heterocyclyl, and -$(CH_2)_m$-Z-(C_1-C_{10} alkyl), where m is 1 to 8 and Z is oxygen or sulfur; or R_1 is a heterocyclyl radical derived from a mono- or poly-cyclic ring containing one to three heteroatoms selected from the group consisting of N, O and S;

R_2 is selected from the group consisting of (C_6-C_{14})aryl-CH_2-, (C_6-C_{14})arylcarbonyl-CH_2-, heteroaryl-CH_2- and heteroarylcarbonyl-CH_2-, wherein said aryl or heteroaryl is unsubstituted or substituted by at least one radical selected from the group consisting of C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_7-C_{12} aralkyl, C_6-C_{10} aryl, C_7-C_{12} alkaryl, hydroxy, C_1-C_{10} alkoxy, C_6-C_{10} aryloxy, C_1-C_{10} alkylthio, C_6-C_{10} arylthio, C_6-C_{10} arylamino, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkenyl, amino, C_1-C_{10} alkylamino, di(C_1-C_{10})-alkylamino, C_2-C_{12} alkoxyalkyl, C_2-C_{12} alkylthioalkyl, C_1-C_{10} alkylsulfinyl, C_1-C_{10} alkylsulfonyl, C_6-C_{10} arylsulfonyl, hydroxy(C_1-C_{10})alkyl, (C_6-C_{10})aryloxy(C_1-C_{10})alkyl, (C_1-C_{10})alkoxycarbonyl, (C_6-C_{10})aryloxycarbonyl, C_2-C_{11} alkanoyl, (C_7-C_{11})aroyl, fluoro(C_1-C_{10})alkyl, oxo, nitro, nitro(C_1-C_{10})alkyl, cyano, cyano(C_1-C_{10})alkyl, aminocarbonyl, (C_1-C_{10})alkylaminocarbonyl, di(C_1-C_{10})-alkylaminocarbonyl, aminocarbonyl(C_1-C_{10})alkyl, aminocarbonyl(C_6-C_{10})aryl, aminosulfonyl, (C_1-C_{10})alkylaminosulfonyl, di(C_1-C_{10})-alkylaminosulfonyl, amidino, carboxy, sulfo, heterocyclyl, and -$(CH_2)_m$-Z-(C_1-C_{10} alkyl), where m is 1 to 8 and Z is oxygen or sulfur; and wherein said heteroaryl is selected from the group consisting of pyrrolyl, furyl, thienyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl thiazolyl, isothiazolyl, pyridyl, 1,3-benzodioxanyl, pyrazinyl, pyrimidinyl, 1,3,4-triazinyl, 1,2,3-triazinyl, 1,3,5-triazinyl, thiazinyl, quinolinyl,

isoquinolinyl, benzofuryl, isobenzofuryl, indolyl, imidazo[1,2-a]pyridyl, pyrido[1,2-a]pyrimidinyl, benzimidazolyl, benzthiazolyl, and benzoxazolyl;

R_3 is hydrogen; and

R_4 is selected from the groups consisting of:

(i) (C_1-C_6)alkoxy(C_1-C_6)alkyl;

(ii) (C_1-C_6)alkyl substituted by a group selected from the group consisting of an amino group $-NR_5R_6$, an ammonium group $-N^+(R_5R_6R_7)$, a hydrazine group $-NR_5-NR_6R_7$, a hydrazonium group $-NR_5-N^+(R_6R_7R_8)$, an ammoniumoxy group $-O-N^+(R_5R_6)$, an imine group $-C=NR_5R_6$, an iminium group $-C=N^+(R_5R_6R_7)$, a guanidine group $-NR_5-C(=NH)-NR_6R_7$, and a guanidinium group $-NR_5-C(=NH)-N^+(R_6R_7R_8)$, wherein each of R_5, R_6, R_7 and R_8 is H, or optionally substituted C_1-C_{10} alkyl or C_6-C_{10} aryl, but excluding a tertiary amino group $-NR_5R_6$, wherein R_5 and R_6 are C_1-C_6 alkyl; and

(iii) (C_1-C_6)alkyl substituted by a 5-7 membered heterocyclic ring selected from the group consisting of pyrrolidine, pyrroline, pyrrol, imidazolidine, imidazoline, imidazole, ~~piperidine~~, dihydropyridine, tetrahydropyridine, pyridine, 1,2-pyrazine, tetrahydropyrimidine, dihydropyrimidine, pyrimidine, 1,4-pyrazine, 1,4-tetrahydropyrazine, 1,4-dihydropyrazine, piperazine, diazepine, oxazolidine, oxazoline, oxazole, morpholino, 1,4-dihydrooxazine, 1,4-oxazine. thiazolidine, thiazoline,

thiaazole, thiomorpholino, 1,4-dihydrothiazine, and 1,4-thiazine; or

R_3 and R_4 together with the nitrogen atom to which they are attached form a 5-7 membered saturated heterocyclic ring containing one or two basic nitrogen atoms selected from the group consisting of pyrrolidine, imidazolidine, piperidine, piperazine, and piperazine substituted at the additional nitrogen atom by C_1-C_6 alkyl or by C_1-C_6 alkyl substituted by halo, hydroxy, C_1-C_6 alkoxy or C_6-C_{10} aryl, or C_2-C_7 alkoxycarbonyl.

81. (Currently Amended) The method according to claim 80, wherein R_1 is selected from the group consisting of pentyl, allyl, phenyl, 4-fluorophenyl, benzyl, 2-furylmethyl and (tetrahydro-2-furyl)methyl;

R_2 is selected from the group consisting of phenyl-CH_2-, 4-methylphenyl-CH_2-, 3-fluorophenyl-CH_2-, 4-fluorophenyl-CH_2-, 3-chlorophenyl-CH_2-, 4-chlorophenyl-CH_2-, phenylcarbonyl-CH_2-, 4-fluoro-phenylcarbonyl-CH_2-, 4-chloro-phenylcarbonyl-CH_2-, 4-pyridyl-CH_2- and 4-oxo-4H-pyrido[1,2-a]pyrimidin-yl-CH_2-;

R_3 is hydrogen; and

R_4 is selected from the group consisting of 2-methoxyethyl, 3-(4-morpholinyl)propyl and ~~3-(1-piperidinyl)propyl~~; or

R_3 and R_4 together with the nitrogen atom to which they are attached form 4-methylpiperazinyl or 1- piperazinyl-4-carboxylic acid ethyl ester.

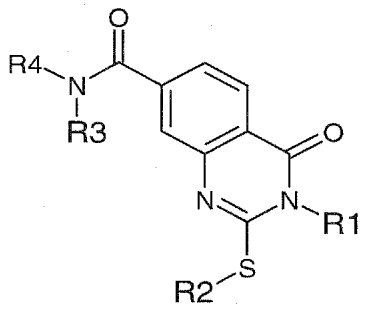
82. (Previously Presented) The method according to claim 46, for the treatment or prevention of inflammatory or autoimmune diseases, disorders or conditions related to cell adhesion or cell migration mediated by heparan sulfate glycosaminoglycans.

83. (Previously Presented) The method according to claim 82, wherein said inflammatory or autoimmune disease, disorder or condition is selected from the group consisting of sepsis, wound associated sepsis, post-septic shock, ischemic leukocyte-mediated tissue damage (ischemia-reperfusion injury) such as myocardial ischemia, platelate-mediated pathologies such as atherosclerosis and clotting, cardiomyopathic disease, stroke, restenosis, infectious meningitis, encephalitis, allergic conjunctivitis, organ/tissue transplant rejection (such as skin, kidney, heart, lung, liver, bone marrow, cornea, pancreas, small bowel, autologous bone marrow transplantation), "graft versus host" disease (GVHD), lupus, frost-bite injury or shock, acute leukocyte-mediated lung injury (such as adult respiratory distress syndrome), asthma, allergic rhinitis, acute pancreatitis, traumatic shock,

traumatic brain injury, acute and chronic inflammation such as atopic dermatitis, psoriasis, contact dermal hypersensitivity and inflammatory bowel disease such as Crohn's disease and ulcerative colitis, rheumatoid arthritis, retinitis; multiple sclerosis; amyloid disorders such as Alzheimer's disease and type II diabetes; angiogenesis pathologies selected from the group consisting of tumor angiogenesis, ophthalmologic disorders such as neovascular glaucoma, diabetic retinopathy, macular degeneration (particularly age-related macular degeneration) and uveitis, reperfusion of gastric ulcer, contraception and inducing abortion at early stages of pregnancy; viral disorders selected from the group consisting of hepatitis C, hepatitis B, influenza, rhinovirus infections, cytomegalovirus infections, AIDS and respiratory syncytial virus infections; bone degradation, osteoporosis, osteoarthritis, kidney disease including glomerulonephritis and nephritis; and bacterial infections.

84. (Previously Presented) The method according to claim 82, wherein said disease is cancer or tumor metastasis.

85. (New) A pharmaceutical composition comprising a pharmaceutically acceptable diluent or carrier and an active ingredient of the general formula I:



wherein:

R_1 is optionally substituted hydrocarbyl or heterocyclyl;

R_2 is selected from the group consisting of H, $(C_1$-$C_{12})$alkyl, $(C_6$-$C_{14})$aryl-CH_2-, heteroaryl-CH_2-, alkylcarbonyl-CH_2-, $(C_6$-$C_{14})$arylcarbonyl-CH_2- and heteroarylcarbonyl-CH_2-;

R_3 and R_4 each is selected from the group consisting of hydrogen, C_1-C_6 alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, and C_1-C_6 alkyl substituted by a group containing a basic nitrogen atom but excluding a tertiary amino group, or by a 5-7 membered heterocyclic ring containing two heteroatoms, one of them being a basic nitrogen atom, or R_3 and R_4 together with the nitrogen atom to which they are attached form a 5-7 membered saturated heterocyclic ring containing one or two basic nitrogen atoms, optionally substituted on the additional nitrogen atom;

and pharmaceutically acceptable salts thereof.